

# UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE		10776-003	5164	
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CUSPA TECHNOLOGY LAW ASSOCIATES			EXAMINER		
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	1820 S.W. 107 AVENUE  MIAMI, FL 33176  BUNNER, BRIDGET E	<u> </u>			
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		1	1647		
			DATE MAILED: 07/30/2002	· /L	

Please find below and/or attached an Office communication concerning this application or proceeding.

		T/	Application No.		Applicant(s)	
•			09/801,115		MA ET AL.	
Office Action Summary			Examiner		Art Unit	
			Daidmot E. Bunner		1647	
	The MAILING DATE of this con	nmunication appe	ars on the cover	sheet with the	correspondence a	ddress
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1)🛛	Responsive to communication	n(s) filed on <u>10 M</u>	lay 2002 .	- 1		
2a)□	This action is FINAL.	2b)⊠ Thi	s action is non-fi	nal.		the merits is
3)	Since this application is in co closed in accordance with the	ndition for allowa e practice under <i>l</i>	nce except for fo Ex parte Quayle,	1935 C.D. 11	, 453 O.G. 213.	
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4)🛛	Claim(s) 1-33 is/are pending	in the application	·	from consider	ration.	
	4a) Of the above claim(s) $6-8$ .		IS/are withdrawi	110111 00110120		
5)	Claim(s) is/are allowed	l.				
6)区	Claim(s) 1-5, 9-10, and 14-16	is/are rejected.				
7)	Claim(s) is/are objecte	ed to.	Latina magniror	nent		
8)🛛	Claim(s) <u>1-33</u> are subject to r	estriction and/or	election requirer	ient.		
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9)🛛	The specification is objected to The drawing(s) filed on	o by the Examine	onted or b)☐ obje	ted to by the E	xaminer.	
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Priority	under 35 U.S.C. §§ 119 and  Acknowledgment is made of	f a claim for foreig	n priority under	35 U.S.C. § 1	19(a)-(d) or (f).	
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	2. Certified copies of the priority documents have been received in Application No  2. Certified copies of the priority documents have been received in this National Stage  3. Copies of the certified copies of the priority documents have been received in this National Stage					
	application from t	ne international L	et of the certified	copies not red	ceived.	
14)	Acknowledgment is made of	a claim for dome:	stic priority unde	r 35 U.S.C. 9	1 19(e) (to a provid	sional application)
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1) 🛛 N	otice of References Cited (PTO-892) otice of Draftsperson's Patent Drawing nformation Disclosure Statement(s) (P	g Review (PTO-948) TO-1449) Paper No(s	,	Notice of Info	ormal Patent Applicati	on (PTO-152)
LLS Patent a	and Trademark Office	065-	Action Summary			Part of Paper No. 12

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### **DETAILED ACTION**

#### Election/Restrictions

Applicant's election with traverse of Group A, claims 1-16, drawn to an isolated polynucleotide in Paper No. 11 (10 May 2002) is acknowledged. Additionally, Applicant's election with traverse of Group 1 (SEQ ID NO: 1; Restriction 2) and Group 5 (SEQ ID NO: 5; Restriction 3) is acknowledged. The traversal is on the ground(s) that the Examiner has not focused upon the two requirements of being independent and distinct. Applicant contends that Groups A-B might present distinct inventions, but each is not independent of the other. Applicant submits that Groups A-B relate to polynucleotides encoding the chemokine-like factor (CKLF) polypeptides and the produced CKLF polypeptides. Applicant states that it is apparent to one skilled in the art that the structures of the CKLF polypeptides of Group B directly depend on the polynucleotides of Group A. Applicant also contends that Groups 1-4 of Restriction 2 and Groups 5-8 of Restriction 3 are not independent of one another. Applicant indicates that the polypeptides have a similarity of structure and community of properties of chemokine-like factors with chemotactic and hematopoietic stimulating activities, and the polynucleotides encodes these similar and related proteins. Applicant asserts that the specification discloses that SEQ ID NOs: 2, 4, 6, and 8 share partial common sequence. Applicant states that the CKLF2, CKLF3, and CKL4 polypeptides are probably allelic gene variants of the CKLF1 polypeptide. Applicant argues that the Markush grouping of the compounds is proper because the substances grouped have a community of chemical and physical characteristics.

This is not found persuasive. As discussed in the previous Office Action (Paper No. 8, 10 April 2002), Groups A and B are independent and distinct from one another. The products of

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Groups A and B are distinct both physically and functionally, and are not required one for the other. For example, the polynucleotide of Group A can be used other than to make the polypeptide of Group B, such as in gene therapy or as a probe in nucleic acid hybridization assays. The polypeptide of Group B can be prepared by processes which are materially different from recombinant polynucleotide expression of Group A, such as by chemical synthesis, or by isolation and purification from natural resources. Each polynucleotide sequence comprising Groups 1-4 and each amino acid sequence comprising Groups 5-8 is a unique sequence requiring a unique search of the prior art. Each polynucleotide listed in Groups 1-4 is a different length and is composed of different nucleic acids, indicating that each encodes a different polypeptide. Further, each polypeptide listed in Groups 5-8 is a different length and is composed of different amino acids, indicating that each is a different polypeptide with diverse functional features. Searching all of the sequences in a single patent application would provide an undue search burden on the Examiner and the USPTO's resources because of the non-coextensive nature of these searches. Therefore, the Examiner has deemed the polynucleotides and polypeptides of Groups A and B independent inventions, each from one another. The Examiner has also deemed the polynucleotide sequences of Groups 1-4 independent from one another and the polypeptide sequences of Groups 5-8 independent from one another.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-8, 11-13, and 17-33 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11 (10 May 2002).

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Claims 1-5, 9-10, and 14-16 are under consideration in the instant application.

#### Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

## Sequence Compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Specifically, sequences in the specification are not accompanied by their relevant sequence identifiers (see pg 23, lines 13-14; pg 24, lines 32-33; pg 25, line 28). Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

## Information Disclosure Statement

- 2. The information disclosure statement filed 02 July 2001 (Paper No. 7) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.
- 3. The information disclosure statement filed 02 July 2001 (Paper No. 7) fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language (see

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document CN 1202906). It has been placed in the application file, but the information referred to therein has not been considered.

### Drawings

4. The drawings are objected to because the lines on the graphs in Figures 5A-5C and 5H-5I cannot be distinguished from one another. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

#### Specification

- 5. The disclosure is objected to because of the following informalities:
- (5a.) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see pg 22, lines 27 and 34; pg 23, line 1). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.
- (5b.) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "NUCLEIC ACID MOLECULE ENCODING CHEMOKINE-LIKE FACTOR 1 (CKLF1)".

Appropriate correction is required.

## Claim Objections

6. Claim 1 is objected to because of the following informalities:

Claim 1 recites non-elected groups.

Appropriate correction is required.

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## 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification, while being enabling for (i) an isolated polynucleotide comprising a polynucleotide encoding the polypeptide as set forth in SEQ ID NO: 2, (ii) a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit No. 0392, (iii) an isolated polynucleotide having the sequence as set forth in SEQ ID NO: 1, and (iv) a polynucleotide capable of hybridizing to the polynucleotide of (i) or (ii), does not reasonably provide enablement for an isolated polynucleotide comprising a naturally occurring variant of the polynucleotide of (i) or (ii) or for an isolated polynucleotide which is at least 85% identical to the polynucleotide of (i) or (ii). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-5, 9-10, and 14-16 recite an isolated polynucleotide comprising (a) a polynucleotide encoding the polypeptide as set forth in SEQ ID NO: 2, (b) a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit No. 0392, (f) a naturally occurring variant of the polynucleotide of (a) or (b), (g) a polynucleotide capable of hybridizing to the polynucleotide of (a) or (b), and (h) a polynucleotide which is at least 85% identical to the polynucleotide of (a) or (b). The claims also recite that the polynucleotide is cDNA, RNA, and genomic DNA. The claims are

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directed to a vector containing cDNA, a host cell, and a method of producing a chemokine-like factor polypeptide.

The specification teaches that fragments of the full length chemokine-like factor (CKLF) gene may be used as a hybridization probe for a cDNA library to isolate the full length CKLF gene and to isolate other genes which have a high similarity to the gene or similar biological activity (pg 8, lines 19-29). The specification also discloses that the terms "fragment", "derivative", and "analog" when referring to the polypeptide of CKLF1 means a polypeptide which retains essentially the same biological function or activity as such polypeptides (pg 10, lines 24-29). The fragment, derivative, or analog of the polypeptide of CKLF or that encoded by the deposited DNA may be one in which one or more amino acids residues are substituted with a conserved or non-conserved amino acid residue, one in which one or more amino acid residues includes a substituent group, one in which the mature polypeptide is fused with another compound, one in which the additional amino acids are fused to the mature polypeptide, and splice variants of the mature polypeptide which are lacking certain amino acid residues (pg 10, lines 32-37; pg 11, lines1-9). However, the specification does not teach variants of the polynucleotide (SEQ ID NO: 1) of the instant application. The specification also does not disclose methods or examples to enable one skilled in the art to obtain a "naturally occurring" polynucleotide that encodes the polypeptide of SEQ ID NO: 2, or any variants of SEQ ID NO: 1, particularly from other besides human.

The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally

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possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct threedimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein and DNA which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

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Relevant literature regarding chemokines reports that the substitution of Tyr<sup>28</sup> and Arg<sup>30</sup> in MCP-1, a CC chemokine, by the corresponding residues in IL-8, Leu and Val, lowers the activity toward monocytes and confers neutrophil chemotactic activity to the CC chemokine (Baggiolini et al. Annu Rev Immunol 15: 675-705, 1997; pg 689, ¶ 4). Furthermore, the replacement of Leu<sup>25</sup> and Val<sup>27</sup> in IL-8 by tyrosines, the corresponding residues of RANTES, or a substitution of Leu<sup>25</sup> by a modified cysteine yield mutants with CC chemokine activity. Baggiolini et al. also disclose that the NH<sub>2</sub>-terminal region of MCP-1 is important for receptor recognition and activation and that the entire sequence of 10 residues preceding the first cysteine is required for full activity. The truncation or elongation of the NH<sub>2</sub>-terminal sequence of MCP-1 leads to loss of activity (pg 689, ¶5).

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity and to obtain a "naturally occurring" variant, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. (Please note that issue of rejection could be overcome by removing the "naturally occurring variant" and "85% identical" language in claim 1(f) and 1(h).)

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8. Claims 1-5, 9-10, and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5, 9-10, and 14-16 recite an isolated polynucleotide comprising (a) a polynucleotide encoding the polypeptide as set forth in SEQ ID NO: 2, (b) a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit No. 0392, (f) a naturally occurring variant of the polynucleotide of (a) or (b), (g) a polynucleotide capable of hybridizing to the polynucleotide of (a) or (b), and (h) a polynucleotide which is at least 85% identical to the polynucleotide of (a) or (b).

The specification teaches a human chemokine-like factor polynucleotide (SEQ ID NO: 1) and a polypeptide encoded by the nucleotides of SEQ ID NO: 1. However, the specification does not teach functional or structural characteristics of the all claimed polynucleotides in the context of a cell or organism. The description of one chemokine-like polynucleotide species (SEQ ID NO: 1) and one polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all variants and fragments and with at least 85% sequence identity to the chemokine-like factor polynucleotide consisting of SEQ ID NO: 1 and the chemokine-like factor polypeptide encoded by SEQ ID NO: 1.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

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whatever is now claimed" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See Vas-Cath at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only, an isolated polynucleotide comprising a polynucleotide encoding the polypeptide as set forth in SEQ ID NO: 2, a polynucleotide having the sequence as set forth in SEQ ID NO: 1, and a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the cDNA contained in CGMCC Deposit No. 0392, and a polynucleotide capable of hybridizing to a polynucleotide at wash conditions of 125mM sodium phosphate (pH 7.2), 0.05 mM EDTA, and 2.5% SDS at 65°C, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas*-

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Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-5, 9-10, and 14-16 are rejected under 35 U.S.C. § 112, first paragraph, as 9. containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The invention appears to employ novel nucleic acid molecules. Since the nucleic acid molecules are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the nucleic acid molecules are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the nucleic acid molecules. The specification does not disclose a repeatable process to obtain the nucleic acid molecules and it is not apparent if the nucleic acid molecules are readily available to the public. It is noted that Applicant has deposited the nucleic acid molecules (p. 9, lines 23-31 of the specification), but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific nucleic acid molecules have been deposited under the Budapest Treaty and that the nucleic acid molecules will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide assurance of

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compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

- (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
- (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
- (d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and
- (e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." At p. 9, the date of the deposit and the name and address of the depository are missing. The specification should be amended to include such, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.

# Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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10. Claims 1-4, 9-10, and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over NCI-CGAP (Genbank Accession No. AI078580) in view of Hillier et al. (Genbank Accession No. AA455042) and Sibson et al. (WO 94/01548).

NCI/CGAP teaches a nucleic acid sequence that is capable of hybridizing to the polynucleotide that encodes the polypeptide as set forth in SEQ ID NO: 2 of the instant application (See sequence alignment attached to this Office Action as Appendix A; see nucleotides 1-452 of NCI-CGAP; see also nucleotides 59-510 of the instant application). It is noted to Applicant that since all DNA will hybridize under conditions of low or no stringency, claim 1(g) reads on every DNA molecule known in the art.

NCI-CGAP does not teach a polynucleotide that encodes the polypeptide as set forth in SEQ ID NO: 2. NCI-CGAP also does not teach expression vectors, host cells, or a method of producing a polypeptide.

Hillier et al. teaches a polynucleotide that encodes the polypeptide as set forth in SEQ ID NO: 2 of the instant application (See sequence alignment attached to this Office Action as Appendix B; see nucleotides 60-356 of Hillier et al. and amino acids 1-99 of SEQ ID NO: 2 of the instant application.)

Hillier et al. does not disclose expression vectors, host cells or a method of producing a polypeptide.

Sibson et al. discloses that it is generally useful to place a desired cDNA sequence into an expression vector, host cell, and express the encoded protein (see pages 8-13).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use NCI-CGAP's and Hillier et al.'s cDNA and the expression vector,

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host cell, and method of expressing and then isolating the encoded polypeptide as taught by Sibson et al. in view of Sibson's suggestion that it would be desirable to do so, as cited above.

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#### Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BEB Art Unit 1647 July 22, 2002 SUPERIOR PATENT STAKINER HELY OLORI CENTRE 1600